REMARKS

Reconsideration and re-examination are respectfully requested. After entering these amendments, claims 1-11, 13, 18, and 33 will be pending.

Claims 15-17 and 20-32 have been canceled, without prejudice, as being drawn to the non-elected invention. Claims 12, 14, and 19 have also been canceled.

Claim 1, as amended, is directed to a crystal comprising an AR-LBD and AR-LBD ligand complex. This amendment to claim 1 is supported by original claim 1.

Claim 5 has been amended to track the amendment to claim 1.

Claims 8 and 9 have been amended to specify that the AR-LBD is mammalian and rat, respectively. These amendments to claims 8 and 9 are supported by original claims 8 and 9.

Claim 10 has been amended to recite that the crystal of claim 1 has unit cell dimensions in angstroms: $a = 56.03 \pm 5\%$, $b = 66.27 \pm 5\%$, $c = 70.38 \pm 5\%$ and an orthorhombic space group P212121. This amendment to claim 10 is supported in the specification from page 5, line 35, through page 6, line 2.

Claims 11 and 13, as amended, are directed to crystals that comprise a molecular complex of an AR-LBD and an AR-LBD ligand. These amendments to claims 11 and 13 are supported by original claims 11 and 13, respectively.

Claim 18, as amended, is directed to a crystal that comprises a molecular complex of an AR-LBD and an AR-LBD ligand, wherein the AR-LBD ligand is in van der Waals contact or hydrogen bonding contact with a ligand binding site of said AR-LBD. This amendment to claim 18 is supported by originally filed claim 18.

Claim 33 has been added to secure enhanced protection for Applicants' invention. The addition of claim 33 is supported in the specification at page 2, lines 19-20 and pages 38-70 (atoms 1-1991) of Table A.

A marked-up version of these amendments is found beginning on a separate sheet entitled "Version With Markings to Show Changes Made." No new matter is believed to be added.

35 U.S.C. 112, first paragraph

Claims 1-14, 18, and 19 stand rejected as purportedly not being enabled by the specification. That rejection is respectfully traversed.

At the outset, Applicants appreciate the acknowledgement in the Office Action that the specification is enabling for a crystal of an AR-LBD complex. (See, Office Action at page 3, first complete sentence.)

Claim 1, as amended, is directed to a crystal comprising an AR-LBD and AR-LBD ligand complex. The specification enables one of skill in the art to make and use the subject matter of amended claim 1, particularly the teachings of the examples (pages 26-37 and Table A on pages 38-

72) providing a crystal AR-LBD and AR-LBD ligand complex. It is further submitted that claims 2-10, which ultimately depend on claim 1, are also enabled.

Claim 11, as amended, is directed to a crystal that comprises a molecular complex of an AR-LBD and an AR-LBD ligand, wherein the AR-LBD has an AR-LBD ligand binding site defined by the structure coordinates of AR-LBD amino acids V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877 and F878 according to Table A. Applicants submit that the specification enables one of skill in the art to make and use the subject matter of amended claim 11, particularly the teaching in the specification of the recited AR-LBD ligand binding site defined by the certain structure coordinates in Table A.

Claim 13, as amended, is directed to a crystal that comprises a molecular complex of an AR-LBD and an AR-LBD ligand, wherein the AR-LBD has a ligand binding site defined by the structure coordinates of AR-LBD amino acids N705, Q711, R752, F764 and T877 according to Table A. It is submitted that the specification enables one of skill in the art to make and use the subject matter of amended claim 13, particularly the teaching in the specification of the recited AR-LBD ligand binding site defined by the certain structure coordinates in Table A.

Claim 18, as amended, is directed to a crystal that comprises a molecular complex of an AR-LBD and an AR-LBD ligand, wherein the AR-LBD ligand is in van der Waals contact or hydrogen bonding contact with a ligand binding site of said AR-LBD and wherein said ligand binding site comprises the structure coordinates of AR-LBD amino acids V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904 or I906 of AR-LBD according to Table A. Applicants submit that the specification enables one of skill in the art to make and use the subject matter of amended claim 18, particularly the teaching in the specification of the recited AR-LBD ligand binding site defined by the certain structure coordinates in Table A.

Withdrawal of these rejections is requested.

35 U.S.C. 112, second paragraph

Claims 11-14 stand rejected as purportedly being indefinite.

With regard to claims 11-14, the Office Action alleges that the recitation of "molecular complex" is indefinite. Claims 11 and 13, as amended, are directed to a crystal that comprises a molecular complex of an AR-LBD and an AR-LBD ligand. It is believed that amended claims 11 and 13 are not indefinite, in view of these amendments to the claims and the definition of "molecular

complex" in the specification at page 8, lines 33-35. Claims 12 and 14 have been canceled, rendering their rejection moot.

With regard to claim 13, the phrase "comprising all or any part of the ligand binding site" cited in the Office Action is not recited in amended claim 13, rendering this rejection moot.

Claims 18 and 19 also stand rejected as purportedly being indefinite. The Office Action alleges that it is unclear what is meant by "binding site." Amended claim 18 specifies that the AR-LBD ligand is in van der Waals contact or hydrogen bonding contact with a ligand binding site of said AR-LBD and wherein said ligand binding site comprises the structure coordinates of the recited AR-LBD amino acids according to Table A. Thus, amended claim 18 specifies that the AR-LBD ligand is in van der Waals contact or hydrogen bonding contact with a ligand binding site of the AR-LBD, and also specifies that the ligand binding site comprises certain structure coordinates. Accordingly, it is submitted that amended claim 18 is not indefinite. Claim 19 has been canceled, rendering this rejection of claim 19 moot.

35 U.S.C. 102

Claims 11-14 stand rejected as purportedly being anticipated by Kuil et al. That rejection is traversed with regard to amended claims 11 and 13, which are directed to crystals that comprise a molecular complex of an AR-LBD and an AR-LBD ligand. It is submitted that Kuil et al. does not disclose the subject matter of amended claims 11 and 13. Claims 12 and 14 have been canceled, rendering their rejection moot. Withdrawal of this rejection is requested.

CONCLUSION

In view of the foregoing amendments and remarks, allowance of the above-referenced application is respectfully requested. The Examiner is invited to contact the undersigned if there are any questions concerning the prosecution of this application.

The Commissioner is authorized to charge Deposit Account 19-3880 (Bristol-Myers Squibb Company) for any requisite fees due or to credit any overpayment.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In showing the changes, deleted material is shown surrounded by brackets and added material is shown by underlining.

IN THE CLAIMS:

1. (amended) A crystal [of an AR-LBD] comprising[:]

[a)] an AR-LBD and [an] AR-LBD ligand complex, [or

b) an AR-LBD without an AR-LBD ligand;]

wherein said crystal diffracts to at least 3 angstrom resolution and has a crystal stability within 5% of its unit cell dimensions.

5. (amended) The crystal of claim 1 wherein [the crystal comprises an AR-LBD and an AR-LBD ligand and] the AR-LBD ligand is an agonist or antagonist, a partial agonist or partial antagonist, or a SARMs of the AR-LBD.

8. (amended) The crystal of claim 1 wherein [said crystal comprises] the AR-LBD is mammalian [AR-LBD protein].

9. (amended) The crystal of claim 1 wherein [said crystal comprises] the AR-LBD is rat [AR-LBD protein].

10. (amended) The crystal of claim 1 [wherein said AR-LBD ligand has the following] having unit cell dimensions in angstroms: $a = 56.03 \pm 5\%$, $b = 66.27 \pm 5\%$, $c = 70.38 \pm 5\%$ and an orthorhombic space group P212121.

11. (amended) A [molecule or molecular complex] crystal that comprises a molecular complex of an AR-LBD and an AR-LBD ligand, wherein [comprising all or any part of] the AR-LBD has an AR-LBD ligand binding site defined by the structure coordinates of AR-LBD amino acids V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877 and F878 according to Table A[, or a mutant or homologue of said molecule or molecular complex].

13. (amended) A [molecule or molecular complex] crystal that comprises a molecular complex of an AR-LBD and an AR-LBD ligand, wherein [comprising all or any part of] the AR-LBD has an AR-LBD ligand binding site defined by the structure coordinates of AR-LBD amino acids N705,

Q711, R752, F764 and T877 according to Table A[, or a mutant or homologue of said molecule or molecular complex].

18. (amended) A crystal that comprises a molecular complex of an AR-LBD and an AR-LBD ligand, wherein the AR-LBD ligand is in van der Waals contact or hydrogen bonding contact with a ligand binding site [in] of said AR-LBD [for an AR modulator in which a portion of said ligand is in van der Walls contact or hydrogen bonding contact with any portion or all of residues] and wherein said ligand binding site comprises the structure coordinates of AR-LBD amino acids V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904 or I906 of AR-LBD according to Table A.